

How frogs and fish can help us learn to freeze humans

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He who shoots first gets frozen longest. Credit: lrosa, CC BY-SA



From Star Wars to Futurama to Alien, the idea that humans can be frozen in time in order to be awoken later is a well-established sci-fi trope. While stopping biological time or inducing long-term hibernation is still as far off as the long-distance space travel that it's associated with in fiction, we can freeze and store cells, tissues and organs, and this is of huge scientific and medical importance.

For example, one of the contributing factors to the shortage of donor organs for transplantation is the challenge of transporting them to the recipient before they have degraded too much. There are also often shortages of blood and plasma, which are needed for nearly all trauma emergencies and routine operations. This need is complicated by their short storage life: up to 42 days for red blood <u>cells</u>, but only eight days for platelets.

Conceptually this is similar to the challenges faced in the frozen food industry: how to maintain even distribution year round, despite uneven supply. Recent advances in <u>stem cell biology</u> and regenerative medicine, along with an ageing population, means the need to store and transport cells and tissue is more important than ever. And much of this comes down to understanding what two thirds of our body is comprised of: water.

Fresh frozen

Back in the 1950s <u>Polge and Lovelock</u> managed to cryopreserve (freeze) sperm cells, which when thawed could be used to fertilise eggs. This was a remarkable achievement and forms the basis for today's IVF treatments and animal farming industries.

Their achievement was overcoming a key problem with freezing cells (or tissue) in that ice tends to form crystals. In fact, water and ice are rather unique. We all know from school that solids are denser than liquids,



which in turn are denser than gases – yet icebergs float. This highlights how ice crystals occupy more space (and therefore have a lower density) than water. This can be lethal when cells are frozen due to the effects of expansion, but also because it concentrates the salt in our cells. To avoid this problem scientists have developed several solutions.

One is to add <u>organic solvents</u> which change the behaviour of water, so that it forms a sort of <u>glass-like substance</u> rather than a crystal, reducing the amount of damage freezing causes. Another is to change the rate of freezing of the cells so as to allow them to dehydrate, which lowers the water content and so the extent of expansion. The success of these methods is seen in the <u>many thousands</u> of successful births from frozen embryos.

Nature's antifreeze

Despite this success, there are many cells and tissues that cannot be frozen, and there would be a clear benefit to reduce the amount of organic solvents added to the cells. Ideally this would be removed altogether before transplantation. So many researchers are now looking to nature for inspiration: several frog species, for example, <u>can survive being frozen solid</u> by producing high concentrations of sugar to protect their cells.

My interest lies in the function of the so called <u>antifreeze glycoproteins</u> that enable fish in the Arctic Ocean <u>to survive in subzero water</u> <u>temperatures</u>.

One of the properties of these proteins is that they not only lower the freezing temperature of water (just as antifreeze for your car does), but they also stop the growth of any ice crystals which form in the fish (or enter it, such as through the gills). The growth of <u>ice crystals</u> during thawing of cryopreserved cells is a huge problem contributing to the



failure of many attempts at freezing. So it seems obvious that adding <u>antifreeze proteins</u> could improve this cryopreservation process.

This is of huge importance and has all sorts of unlikely applications. For example, our tongues can detect crystals around 50 microns in size, so the ice cream industry would like to ensure that all ice is smaller than this to improve texture (and there has been a huge amount of research into additives, known as ice structuring proteins, to achieve this).

But as is often the case, there is a problem. Antifreeze proteins are expensive and not easy to chemically synthesize. To address this my research team and others have developed synthetic polymers – water soluble plastics – which can perform the same function as antifreeze proteins. Remarkably, when we add these to blood cells we can see a <u>clear improvement in their cryopreservation</u> which we hope will one day help us to improve the storage of a huge range of cell types.

Next time you add an ice cube to your drink and it floats to the top, think about how remarkable that is. Also consider how remarkable it is that life can flourish in sub-zero temperatures, when we don hats and coats once the days get shorter. By appreciating these facts, we can appreciate the wonder of evolution, and also ask interesting scientific questions which one day might help us save lives or one day, store ourselves. Though, at the moment, that is still closer to science fiction than science fact.

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